REMARKS

The Claim Amendments

Applicants have amended claim 1 to recite an isolated polynucleotide encoding a human hPXR polypeptide or fragment thereof, wherein the polynucleotide comprises the nucleotide sequence of SEQ ID NO: 112 and wherein the polypeptide or fragment thereof has an impaired transcriptional activity upon rifampicin treatment compared to a wild-type hPXR polypeptide. These amendments are supported throughout the specification, e.g., page 37, lines 9-11, Figure 6 and Example 4, generally.

Applicants have amended claim 34 to recite a primer or probe consisting of an oligonucleotide comprising a fragment of the polynucleotide of claim 1 or a fully complementary sequence thereof wherein said fragment comprises SEQ ID NO:112. This amendment improves the form of the claim.

These claim amendments are made expressly without waiver of applicants' rights to file for and to obtain claims directed to the cancelled or amended subject matter in this application or subsequent applications claiming benefit herefrom.

None of the amendments to the claims constitutes new matter. Their entry is requested. Upon entry of these amendments, claims 1, 4-8, 34, 36 and 37 are now pending in this application.

Office Action

Former Objections

Applicants thank the Examiner for her reconsideration and withdrawal of the former objections to the specification as well as to form of the claims.

The Rejections

35 U.S.C. §112, First Paragraph – Written Description

Claims 1, 4-8, 34 and 36-37 stand rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. The Examiner states that the claim is drawn to a polynucleotide that encodes a variant hPXR protein or fragment thereof, without reciting any particular biological activity or other distinguishing feature. The Examiner therefore contends that the claim is drawn to a genus of nucleic acids that is defined solely by sequence identity and there is not sufficient written description of the claimed genus.

Pursuant to a telephone interview between the undersigned and Examiners Chandra and O'Hare on April 19, 2006, and a follow up telephone conference with Examiner Chandra on May 17, 2006, applicants have agreed to amend independent claim 1, and the claims that depend therefrom, to recite that the polypeptide or fragment thereof has an impaired transcriptional activity upon rifampicin treatment compared to a wild-type hPXR polypeptide. This claim amendment is fully supported by the specification, as indicated above. This

amendment obviates the Examiner's objection to the above-identified claims. Applicants request that the Examiner reconsider and withdraw this objection.

35 U.S.C. §102 – Anticipation

Hwang (§102(b)) and Mittman (§102(e))

Claim 1 stands rejected under 35 U.S.C. §102(b) as anticipated by Hwang et al., Genomics 30:293298, 1995: Accession R57588, GI: 827441 ("Hwang"). Claims 1, 4-8, 34, and 36-37 stand rejected under 35 U.S.C. §102(e) as anticipated by Mittman et al., U.S. Patent 6,821,724 ("Mittman"). The Examiner states that Hwang teaches a polynucleotide sequence GI:827441 that is 100% identical to the polynucleotide sequence of SEQ ID NO:112. The Examiner states that Hwang reads on claim 1 because the claim does not require any functional limitation for the hPXR variant or its fragment. The Examiner also states that Mittman refers to a polynucleotide sequence that is 100% identical to the sequence of SEQ ID NO:112. Applicants traverse.

Claim 1, prior to the amendment made herein, was directed to an isolated polynucleotide encoding a variant human pregnane X receptor (hPXR) polypeptide or fragment thereof wherein the polynucleotide comprises the nucleotide sequence of SEQ ID NO: 112. As stated earlier, applicants have discovered phenotypic changes associated with an amino acid substitution resulting from a nucleotide change in a variant of the hPXR gene. A portion of the hPXR nucleotide sequence containing the polymorphism that produces the variant polypeptide

with impaired transcriptional activity is provided in SEQ ID NO: 112. Neither Hwang nor Mittman describe or refer to an hPXR polypeptide. Neither of the sequences referred to in Hwang and Mittman is within an hPXR-encoding sequence. These documents, therefore, cannot anticipate the subject matter of a claim directed to an isolated polynucleotide that comprises the nucleotide sequence of SEQ ID NO: 112 and encodes a variant human pregnane X receptor (hPXR) polypeptide or fragment.

However, in the interest of advancing prosecution, applicants have even further obviated the above rejections. As amended, claim 1 recites that the variant hPXR polypeptide or fragment has an impaired transcriptional activity upon treatment with rifampicin compared to a wild type hPXR protein. Applicants have also amended claim 34 to recite that the primer or probe consists of an oligonucleotide comprising a fragment of the polynucleotide of claim 1 or a fully complementary sequence thereof. Applicants therefore request that the Examiner withdraw these objections.

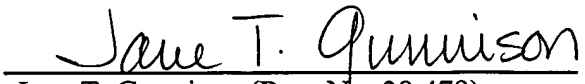
Rejoinder

Applicants request that if the claims are found to be allowable that claim 22, directed to a method of using the polynucleotide of claim 1, be rejoined.

Conclusion

Applicants request favorable consideration and early allowance of the elected claims.

Respectfully submitted,



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